
Dear Editors and reviewer of *World Journal of Clinical Cases*,

Thank you very much for your kind and instructive comments for our submitted manuscript (No: 65537, Title: "Primary hepatic neuroendocrine tumor: a case report with 18F-FDG PET/CT findings"). Revision has been made according to the comments from the one reviewer and the editorial office. All the changes to the text have been marked in red.

Responses to Reviewer #1:

1. In the discussion, the authors can expand the discussion how they excluded the possibility of the liver NET was not metastasis?

2. Pathologic diagnosis is critical for this case. Although beautiful histologic pictures are seen with this paper, but there is no pathologic description in the case report, which should be added. Also the authors need to add 2 more very common markers: CDX2 and TTF1, and if there is, Islet1 and/or PAX8 IHCs should be added. Although these markers are not 100% specific, if CDX2 positive, which might more point this NET might be metastatic from small bowel or appendix. Others such as PAX8/Islet1 and TTF-1 might more point to pancreas or lung primary. In the discussion, the authors also need to discuss why pathologically this liver tumor is primary not metastatic. This discussion can be combined with my comment 1.

Response: Thank you for your kind suggestions. The pathologic description, CDX-2 and TTF1 results have been added in the manuscript (Page 4) and listed as follows: "Histological examination demonstrated a well-differentiated neoplasm with the trabecular and glandular architectural pattern. The Ki-67 proliferation index was about 15% in tumor cells. Immunohistochemical staining revealed positive immunoreactivities for CD56, cytokeratin (CK) AE1/AE3, synaptophysin (Syn), and negative immunoreactivities for CDX-2, chromogranin A (CgA), thyroid transcription factor (TTF-1). " Markers of PAX8 IHCs and Islet1 were not tested in immunohistochemical examinations. We also have discussed why they excluded the possibility of the liver NET was

not metastasis in the manuscript (Page 6) and listed as follows:” In this study, immunohistochemical examinations revealed positive immunoreactivities for CD56, CK AE1/AE3, Syn, which confirmed the tumor was a NEN. Negative expressions of CDX-2 and TTF-1 helped rule out the possibility of small bowel, appendix, lung, and thyroid origins. Thus, we confirmed the diagnosis by histology and imaging methods, such as ¹⁸F-FDG PET/CT.“

3. This patient was received aggressive treatment. This patient had no symptoms and the tumor growth was very slow. Why not a conservative management was given. The authors need to discuss the indication for the aggressive treatment for this patient.

Response: Thank you for your insightful comment. The reason why the patient was received aggressive treatment has been integrated into the discussion according to your comment as follows (Page 7):” After one course of TACE, no decrease of the tumor size was observed, and the patient’s serum levels of CEA, CA19-9, and CA12-5 were increased. The ENETS consensus Guideline for the standards of care in NEN suggests that chemotherapy might be considered in NETs of other sites (lung, stomach, colon, etc.) when the Ki-67 is at a high level (upper G2 range) or after failure of other therapies^[15]. Under these circumstances, the patient received three courses of chemotherapy, and partial response was achieved.“

4. I would suggest to give the exact numbers of the laboratory tests instead of just saying elevated (The blood serum levels of tumor markers (CEA, CA19-9, and CA12-5) were elevated).

Response: Thank you for your helpful suggestion. The exact numbers of the blood serum levels of tumor markers before and after the treatment have been added to the manuscript and listed as follows:” The blood serum levels of CEA (5.4 ng/mL; reference range 0--4.7), CA19-9 (52.4 U/mL; reference range 0--27), and CA12-5 (141 U/mL; reference range 0--35) were elevated. The

alpha fetoprotein (AFP) serum level was normal.” ,and “The patient’s blood serum levels of CEA (5.9 ng/mL; reference range 0--4.7), CA19-9 (109.2 U/mL reference range 0--27), and CA12-5 (166 U/mL reference range 0--35) were elevated. Abdominal MR images showed no decrease in tumor size. Thus, the patient was treated by three courses of chemotherapy.”

Response to Science editor:

1 Scientific quality: The manuscript describes a case report of the primary hepatic neuroendocrine tumor. The topic is within the scope of the WJCC. (1) Classification: Grade C; (2) Summary of the Peer-Review Report: The authors reported one primary liver NET case, which is very rare, and it is a diagnostic exclusion. The questions raised by the reviewers should be answered; (3) Format: There are 3 figures; (4) References: A total of 14 references are cited, including 3 references published in the last 3 years; (5) Self-cited references: There is no self-cited reference; and (6) References recommendations: The authors have the right to refuse to cite improper references recommended by the peer reviewer(s), especially references published by the peer reviewer(s) him/herself (themselves). If the authors find the peer reviewer(s) request for the authors to cite improper references published by him/herself (themselves), please send the peer reviewer’s ID number to editorialoffice@wjgnet.com. The Editorial Office will close and remove the peer reviewer from the F6Publishing system immediately. 2 Language evaluation: Classification: Grade B. A language editing certificate issued by Editage was provided. 3 Academic norms and rules: The authors provided the written informed consent. No academic misconduct was found in the Bing search. 4 Supplementary comments: This is an unsolicited manuscript. No financial support was obtained for the study. The topic has not previously been published in the WJCC.

Response: Thank you very much for your positive summary and evaluation. Related content has been added to the revised manuscript.

5 Issues raised: (1) The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor. 6 Recommendation: Conditional acceptance.

Response: Thank you for your advice. The original figure document has been uploaded together with the revised manuscript.

Response to Company editor-in-chief:

I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Clinical Cases, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. Before its final acceptance, the author(s) must provide the Signed Informed Consent Form(s) or Document(s). For example, authors from China should upload the Chinese version of the document, authors from Italy should upload the Italian version of the document, authors from Germany should upload the Deutsch version of the document, and authors from the United States and the United Kingdom should upload the English version of the document, etc.

Response: Thank you for your kind suggestion. The Signed Informed Consent Form has been uploaded together with the revised manuscript.